

47. (Amended) A system of associated devices for preparing oligonucleotide compounds targeted to a nucleic acid and identifying specific members of said oligonucleotide compounds that possess at least one property, said system comprising:

a first device preparing a virtual library of oligonucleotide compounds in computer manipulable form from a selected target nucleic acid sequence;

a second device comprising an automated synthesizer accepting said computer manipulable form and preparing a corresponding set of real oligonucleotide compounds; and

a third device accepting said set of real oligonucleotide compounds and performing at least one assay for each of said real oligonucleotide compounds wherein said assay identifies the specific members of said set possessing said at least one property, and wherein said assay is performed by computer-controlled real-time polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

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48. (Amended) The system of claim 47 wherein the steps of [preparing a virtual library,] preparing a real library and performing at least one assay are performed robotically.

--59. A system of associated devices for preparing oligonucleotide compounds targeted to a nucleic acid and identifying specific members of said oligonucleotide compounds that possess at least one property, said system comprising:

a first device preparing a virtual library of oligonucleotide compounds in computer manipulable form from a selected target nucleic acid sequence;

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a second device comprising an automated synthesizer accepting said computer manipulable form and preparing a corresponding set of real oligonucleotide compounds; and

a third device accepting said set of real oligonucleotide compounds and performing at least one assay for each of said real oligonucleotide compounds wherein said assay identifies the specific members of said set possessing said at least one property, wherein said property is the ability to modulate a target nucleic acid sequence.

60. The system of claim 59 wherein the steps of preparing a real library and performing at least one assay are performed robotically.
61. The system of claim 59 wherein at least one device reduces the members of said virtual library by eliminating members based on a set criteria.
62. The system of claim 59 wherein at least one device reduces the members of said virtual library by a process of selection based on a uniform distribution of oligonucleotide compounds across the selected nucleic acid target.
63. The system of claim 59 wherein at least one device applies selected chemical modifications to said virtual oligonucleotide compounds to give chemically modified virtual oligonucleotide compounds in computer manipulable form.
64. The system of claim 63 wherein selected chemical modifications are applied to each of said virtual oligonucleotide compounds electronically.
65. The system of claim 59 wherein said target nucleic acid sequence is that of a genomic DNA, a cDNA, a product of a polymerase chain reaction, an expressed sequence tag, an mRNA or a structural RNA.
66. The system of claim 59 wherein said target nucleic acid sequence is a human nucleic acid sequence.
67. The system of claim 59 further including a fourth device assaying at least one biological property of said oligonucleotide compounds, wherein said third device assays at least one physical or chemical property.--

REMARKS

Claims 47-58 have been examined in the present application. Claims 47 and 48 have been amended, claims 49 and 51 have been cancelled, and new claims 59-67 have been added herein. Upon entry of the present Amendment, claims 47, 48, 50, and 52-67 will be pending.

I. The Claimed Inventions Are Novel**A. The Gilbert Reference**

Claims 47, 48, 50, and 52-58 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by EPO 0,514,927 (hereinafter, the "Gilbert reference"). Although Applicants disagree with the assertions in the Office Action and maintain that the claimed inventions are novel, solely to advance prosecution of the present application, Applicants have amended the claims. In particular, claim 47 has been amended to incorporate the subject matter of claim 49, which was not rejected in view of the Gilbert reference. Applicants reserve the right to prosecute the subject matter of claim 47, prior to amendment herein, in another application. Thus, claims 47, 48, 50, and 52-58 are novel. Accordingly, Applicants respectfully request that the rejection of claims 47, 48, 50, and 52-58 under 35 U.S.C. §102(b) be withdrawn.

B. The Hubbell Reference

Claims 47, 48, 50, and 54-57 are rejected under 35 U.S.C. §102(b) and (e) as allegedly being anticipated by U.S. Patent No. 5,571,639 (hereinafter, the "Hubbell reference"). Although Applicants disagree with the assertions in the Office Action and maintain that the claimed inventions are novel, solely to advance prosecution of the present application, Applicants have amended the claims. In particular, new claims 59-67 have been added in which the subject matter of claim 51, which was not rejected in view of the Hubbell reference, has been incorporated into claim 47. Again, Applicants reserve the right to prosecute the subject matter of claim 47, prior to amendment herein, in another application. Thus, claims 47, 48, 50, and 54-57 are novel. Accordingly, Applicants

respectfully request that the rejection of claims 47, 48, 50, and 54-57 under 35 U.S.C. §102(b) and (e) be withdrawn.

II. The Specification Contains Sufficient Written Description

Claims 47-58 are rejected under 35 U.S.C. §112, first paragraph for allegedly failing to provide sufficient written description. Applicants traverse the rejection and request reconsideration thereof because the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

The Office Action mistakenly asserts that the specification lacks support for the specific citation of the three devices recited in claim 47 and, thus, recitation of three devices is new matter. It is established law that limitations appearing in claims need not be literally recited in the specification. The issue is not whether words used in the claims are present in the specification but, rather whether the concept expressed by the words is present. *In re Anderson*, 176 U.S.P.Q. 331 (C.C.P.A. 1973). Applicants teach at, for example, page 8, line 2 of the specification, that the present invention is directed, in part, to "systems" for implementing the methods of the invention. The term "system" is defined, for example, as a "group of interacting, interrelated, or independent elements forming a complex whole." (See, page 1234 of *The American Heritage Dictionary*, a copy of which is provided herewith). Thus, Applicants submit that one skilled in the art would understand that Applicants were, in fact, in possession of a system comprising devices or apparatus recited in the claims at the time the application was filed.

The first device for preparing a virtual library is described at, for example, page 14, line 28 to page 19, line 34 of the specification. Applicants teach assembly of target nucleotide sequences using, for example, computerized homology search algorithms and sequence fragment assembly algorithms to search databases. Indeed, Applicants teach in Table 1 numerous databases that can be searched by computer programs such as BLAST or Gapped BLAST. Applicants also teach that a set of nucleobase sequences can be generated *in silico* based upon the target nucleotide sequence.

Applicants teach that a virtual oligonucleotide chemistry is applied to the nucleobase sequences in order to yield a set of virtual oligonucleotides that can be evaluated *in silico*. Further, Applicants teach at, for example, page 61, line 33 to page 62, line 11 of the specification and in Figures 18 and 19, that computer servers are provided for storing chemical structures, and sample tracking and that a compute engine runs computational programs for oligonucleotide walking, for example. Thus, when Applicants' teachings are taken as a whole, a computerized device for assembling target molecules and applying virtual oligonucleotide chemistry to the assembled targets is taught in Applicants' specification. As recognized by the Examiner, the second device for automated synthesis is described in the specification at, for example, page 39, line 14 to page 52, line 18. Indeed, Figures 23 and 24 describe one particular embodiment illustrating an apparatus for synthesizing oligonucleotides. Devices for performing hybridization or immunoassay type assays are, as recognized by the Examiner, described in the specification. Additional devices for performing assays are described at, for example, page 61, line 33 to page 62, line 38 of the specification wherein Applicants teach that preferred systems include instruments and workstations including, for example, an optical density reader, a combined liquid chromatography and mass spectroscopy instrument, a gel fluorescence and scintillation imaging system, a capillary gel electrophoresis system, and a real-time PCR system. Thus, the concept of a plurality of devices for preparing virtual oligonucleotides, for automated synthesis of oligonucleotides and for performing assays is disclosed in the specification.

The Office Action incorrectly asserts that claim 58, which recites a fourth device for assaying at least one biological property, is not supported by the specification. Applicants teach at, for example, page 55, line 13 to page 58, line 32 of the specification that the synthesized oligonucleotides can be assayed for activity using numerous cell lines by methods such as Northern blot analysis, competitive PCR, or reverse transcriptase PCR. Thus, Applicants teach a fourth device that can be used to assay a biological property of an oligonucleotide.

Claim 48 has been amended to no longer recite that the preparation of a virtual library is performed robotically.

Claim 52 recites that at least one device reduces the members of the virtual library by eliminating members based on a set criteria. Applicants teach in, for instance, Example 14 of the specification eliminating members of a virtual library based on a set of criteria. Claim 53 recites that at least one device reduces the members of the virtual library by a process of selection based on a uniform distribution of oligonucleotide compounds across the selected nucleic acid target. Applicants teach at, for example, page 25, line 35 to page 26, line 22 of the specification, reduction of the members of the virtual library by a process of selection based on a uniform distribution of oligonucleotide compounds across the selected nucleic acid target. Thus, claims 52 and 53 are sufficiently supported in the specification.

Claims 54 and 55 recite, in part, chemical modifications of virtual oligonucleotide compounds, support for which can be found at, for example, page 18, lines 21-26, where Applicants teach that steps 300 and 400 can be performed in any order when generating a set of nucleobase sequences *in silico*. Further, page 26, line 23 to page 39, line 13 is replete with chemical modifications to the base, sugar and internucleoside linkage that can be used in the present invention. Thus, the chemical modifications recited in claims 54 and 55 are sufficiently supported in the specification.

In view of the foregoing arguments, the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Accordingly, Applicants respectfully request that the rejection of claims 47-58 under 35 U.S.C. § 112, first paragraph, be withdrawn.


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PATENT

III. Conclusion

In view of the foregoing, Applicants submit that the claims presently before the Examiner are in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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Enclosure: page 1234 of The American
Heritage Dictionary

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